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SOME NEUROLOGICAL OBSERVATIONS IN 150 LAMINECTOMIES FOR SPINAL DISEASE AND INJURY.[1]

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During the past six years I have had the occasion to make a number of observations upon 150 patients with diseases or injuries of the spinal cord who were subjected to surgical interference. Some of the observations are here recorded, so that others may check up our results and report upon their own experiences.

Root Pains in Spinal Disease. Pearce Bailey and Joseph Collins have recently published papers in which they point out that frequently extramedullary spinal disease has, contrary to the general opinion, a painless beginning, while intramedullary disease may be characterized by the early appearance of root pains. Many of the cases reported by these authors were operated upon by the writer, and very often the operative findings gave the explanation for the presence or the absence of early root pains.

Thus we have found that in extramedullary tumors which develop under a slip of the dentate ligament, root pains are often missed among the early symptoms. The explanation for this is to be found in the anatomical relations between the dentate ligament and the posterior roots. The ligament lies in front of the posterior

[1] Read at the Meeting of the Section for Nervous and Mental Diseases, New York Academy of Medicine, October 10, 1910.

roots, and it is easy to understand that the latter are, to a considerable degree, protected against pressure from in front by the interposed dentate ligament.

We have made the interesting observation that large tumors are softer in consistency than the small ones, and are less apt to cause marked cord symptoms until the growth has attained a very large size. The small tumors, on the other hand, are often very hard, and rapidly exert considerable pressure upon the cord. Some of the large soft tumors do not cause pressure upon the nerve roots for a long time, and in cases of this kind, root pains as early symptoms are often wanting. In the large soft growths which surround the roots of the cauda equina (giant endotheliomas) early root pains are likewise relatively infrequent. It is surprising how little pain is complained of by a patient in whom the lower end of the spinal canal is filled with soft tumor growth which surrounds and envelops all of the nerves of the cauda equina.

I have operated upon several patients with small extramedullary growths on the posterior surface of the cord, who gave no history of pain as an early symptom of their disease. In these patients the tumor lay in the mid line of the cord on its posterior surface and had not attained a sufficient size to compress the origins of the posterior roots on either side. It is well known that excepting for the lines of attachment of the posterior roots, the spinal cord is not sensitive to pain, and the explanation for the painless early course in some patients with small extramedullary new growths is to be found in this insensitiveness of the cord tissue.

In intramedullary spinal tumors, on the other hand, early root pains do occur, and we have seen and operated upon two patients in whom the localized swelling of the cord from the growth occurred under a posterior root, so that the root was stretched very early and root pains were complained of among the earliest symptoms of the disease.

I do not wish to be understood as denying that early root pain is most frequent in extramedullary tumors and is relatively rare in intramedullary new growths, but the exceptions to this rule are so numerous, that one can not rely upon this symptom alone to differentiate between diseases which begin outside of or within the cord tissue.

The Sensory Symptoms in Spinal New Growths. In the majority of instances, a spinal disease which causes spastic paraplegia without any disturbance of sensation, is to be classed as a degenerative process in the motor pathways of the cord, but frequent exceptions to this rule occur. For example, I have operated upon a young woman and removed a large soft glioma which lay in the median line on the posterior surface of the cord in the upper dorsal region, in whom repeated careful examinations by experienced neurologists failed for many months, to find any sensory disturbance

at all. The history of this patient is of sufficient interest to report in detail:

Large extramedullary tumor of cervical cord; laminectomy and removal; cure.

Annie R., aged nineteen years, admitted to the surgical service of Dr. Sachs, at Mt. Sinai Hospital, on May 16, 1913. The patient had been seen for a number of months by Dr. Abrahamson, because of the complaint of a feeling of weakness in both lower limbs. Examination showed that the lower limbs were somewhat weak and that the knee and ankle-jerks were slightly exaggerated. There were no sensory disturbances of any kind. Three months before admission, the patient fell to the ground and when she was picked up, she found that her right leg was much weaker than her left leg. From this time on the weakness grew gradually more marked and the right leg became increasingly stiff. The left leg has also become somewhat stiff and weak. Since her fall, the patient has had urgency of urination with occasional loss of control of the vesical sphincter.

Physical Examination on Admission. The patient was a healthy looking young woman. Cranial nerves normal. Power in upper limbs good; reflexes not exaggerated; equal on both sides. Abdominal reflexes were present and equal. Power in lower limbs poor, but the right is much weaker than the left. Both limbs were very spastic. Knee-jerks exaggerated, right greater than left; ankle-jerks exaggerated, bilateral ankle clonus and Babinski. Wassermann and roentgen ray negative. Careful examination failed to reveal a disturbance of sensation in any part of the body.

May 18. A lumbar puncture was done and 6 c.c. of clear yellow fluid not under increased pressure were removed. After the spinal puncture, the patient began to complain of pain in the right shoulder.

May 20. Today, for the first time, there is some diminution in pain and temperature sensation up to the level of the second dorsal area, most marked on the left side. Tactile sensation is normal all over the body.

May 21. There is now complete loss of pain and temperature sensation up to the second dorsal level, but light touch is distinctly felt over the affected areas. Deep muscle sense is also not affected.

May 22. Today, for the first time, there is some diminution of tactile sensation below the area of distribution of the second dorsal segment, and more marked on the left side of the body. By evening of the same day, there was complete anesthesia over the affected areas, and the patient was transferred to the Surgical Service for immediate operation.

Laminectomy was performed on the same evening, by Dr. Elsberg, and a large soft tumor was exposed which lay on the posterior surface of the cord and was so closely connected with the cord that its removal was put off for a second operation. Two weeks

later, the wound was reopened, and the large soft, well encapsulated growth was easily removed. It was 6 cm. in length and at least 1 cm. in width. Pathological report was glioma. Convalescence was uneventful. Within two months most of the motor and sensory symptoms had disappeared, and one month later she was entirely well.

As I have already mentioned, in the large soft tumors which grow around the conus and the roots of the cauda equina, sensation in the lower extremities is either normal or the changes are so slight that the examiner is often in doubt as to the reality of the slight sensory changes. It is most surprising, after the examination has failed to reveal marked sensory disturbances in the lower limbs, to find at operation a large tumor which fills up the lower part of the spinal canal and has grown between and around the nerves of the cauda equina. The absence of sensory disturbances can only be explained on the basis of the soft consistency of the new growth.

Many benign extradural tumors cause for a long time, very vague and indefinite sensory changes. I have operated upon several patients in whom the diagnosis of spinal cord tumor was not made for a long time because of the slight and irregular sensory disturbances. The following patient was watched in the out-patient department of the New York Neurological Institute for many months by Dr. E. L. Zabriskie and by the writer. Distinct objective sensory changes were found long after motor cord symptoms had already been prominent.[1]

Extradural Fibroma of Cord; Laminectomy and Removal. Cure. A. K., aged eighteen years, first came to the out-patient department of the New York Neurological Institute in September, 1913. For three months his friends had told him that he walked with a staggering gait and he himself noticed that he was unsteady on his feet. Several times he was so unsteady that he fell to the ground. This was his only complaint. He was examined by Dr. Zahriskie, but aside from an unsteadiness when he walked, nothing abnormal could be discovered. The patient entered the hospital and repeated careful examinations were made. The reflexes were normal, power in the lower limbs good, no evidence of any sensory disturbance. In October the reflexes in the lower limbs became exaggerated and he developed ankle clonus and Babinski on the left side. At this time there were irregular and very indefinite areas of disturbed sensation on the anterior surfaces of both thighs. After a few weeks stay in the hospital, the patient was discharged and returned to the out-patient department at regular intervals. For a number of months, he was watched by Dr. Zahriskie but no definite areas of disturbed sensation could be made out. In December, 1913, his

[1] I am indebted to Dr. Collins and Dr. Zabriskie for permission to publish this case.

condition grew worse, walking became more difficult so that by the beginning of January, 1915 (seven months from onset of his illness) he was unable to walk or stand unless supported. About this time he began to complain of pain in the right side of the abdomen. He was readmitted to the institute on the service of Dr. Collins on February 11, 1914.

Physical examination now showed the following: The abdominal reflexes were present and equal. The cremasterics could not be obtained. Knee- and ankle-jerks exaggerated, left more than right; exhaustible ankle clonus on left side; Babinski and Chaddock on left. Complete loss of deep muscle sense in left lower extremity. The patient has lost all power in the lower limbs except for slight flexor power at the left knee. The sensory disturbances are very indefinite. There seems to be a slight diminution in tactile and pain sense up to the level of the twelfth dorsal segment. The sensory loss is more distinct over the outer surface of the left leg. It is difficult to say with certainty that there is any disturbance of temperature sense, but it is very slight at the best.

Laminectomy, February 14, 1914 (by Dr. Elsberg): Removal of spinous processes and laminæ or dorsal ninth, tenth, and eleventh. To the right of the tenth dorsal segment, outside of the dura was a bluish tumor mass over which a nerve root was tightly stretched. After division of the nerve root, the growth was easily removed. Convalescence uneventful. All of the symptoms rapidly improved. The patient was presented at the meeting of the New York Surgical Society in April (two months after the operation) subjectively well. One month later, physical examination failed to show any evidence of the previous motor and sensory disturbances. The tumor was reported a fibroma.

Remarks. This case presents a number of features of interest. The presence of motor symptoms long before the appearance of any evidence of sensory disturbance is unusual. When the sensory disturbances finally appeared, they were very indefinite and irregular. Root pain (pain in the right side of the abdomen) appeared only seven months from the beginning of his illness in spite of the fact (as demonstrated at the operation) that the eleventh dorsal root was stretched over the tumor. Finally, the fact of most marked motor disturbance on the opposite side, is of great interest. We have observed this in several instances. It is to be explained by a kind of contrecoup. The spinal cord was pushed to the left by a tumor on its right side, so that the left side of the cord was pressed against the bony wall of the spinal canal resulting in more interference with the left than with the right pyramidal tracts.

Several years ago we had under observation a patient in whom the diagnosis of multiple sclerosis was finally made, in whom sensory disturbances were most marked on the anterior surface of the body.

Since that time, we have examined a number of patients who suffered from a variety of diseases (extradural and intradural tumors, disseminated sclerosis, syringomyelia, stab wound of the cord) in whom the sensory changes on the anterior surface of the body were more marked than on the posterior surface. In several patients, with slight but distinct hypesthesia and hypalgesia on the anterior surface of the trunk and lower limbs, the sensation on the posterior surface was normal. If the diminution of feeling over the front of the body was very marked, that on the back was often much less distinct. I have never, however, seen any difference between the anterior and posterior surfaces of the body when the sensation on the anterior has been entirely lost. While this observation may have been recorded by others, the only reference to the subject I have been able to find is one by Redlich (Neurologisches Centralblatt, 1915, No. 22) who noticed a difference between the sensory disturbances over the front and the back of the trunk in some cases of cerebral hemianesthesia. Recently I operated upon a patient who had a well marked Brown-Sequard syndrome from a stab wound of the back. There was distinct sensory loss affecting all three sensations up to the level of the sixth dorsal segment in front, while, on the back, the loss of sensation was so slight that there was some doubt whether the sensory loss was real or not. At the operation a knife blade two inches long was removed from the spinal canal. It had partially divided the lateral third of the cord.

In a number of patients, also, we have noted that, if pain and thermal sensation was diminished—the disturbance of thermal sense was more marked than that of pain sense. In many cases of spinal compression sensitiveness to pain was markedly diminished over definite areas, while the recognition of and the differentiation between hot and cold was lost entirely.

OBSOLETE MILIARY TUBERCLES OF THE SPLEEN.

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Tuberculosis of the spleen is most commonly observed in cases of widespread miliary tuberculosis. In the not uncommon miliary disease of children and early adolescence, the spleen is usually involved in an intense infection of its tissues. Under these conditions the localization of the infection is mainly through a filtration of the blood by the spleen. The spleen, however, becomes only one of the many tissues in which the microörganisms locate.

The tubercles which arise through the activity of this infection are all of about the same age, showing fairly uniform characters and common stages of development. At autopsy these lesions are seen in the acute or subacute stages, and are scattered in innumerable quantities through the spleen pulp.

The spleen also has been found to be the seat of primary tuberculosis. In the use of the term "primary" it is not meant that the spleen is the portal entry or even the first lesion induced by the invasion of the tubercle bacillus. The term is rather meant to suggest that the pathological process brought about in the spleen is more marked than found elsewhere, and not uncommonly the advanced tuberculous lesion of the spleen leads to a further dissemination into other parts. Thus not a few cases of the so-called primary tuberculosis of spleen show evidence of an older lesion in the thorax with, it may be, very recent tubercles in other tissues. The splenic lesion thus lies intermediate in time and has antedated some of the tuberculous processes of other organs. Not a few of the cases of primary tuberculosis of the spleen have been observed clinically and have received surgical intervention by splenectomy. In these cases it is obvious that although the splenic manifestations have been most prominent during life, no definite information can be offered as to the sequence of events in the tuberculous process. It is interesting that in these cases of primary tuberculosis of the spleen the organ is often found definately enlarged.

To this group of tuberculous infections of the spleen must be added the one here under discussion, the healed or partially healed miliary lesion. Little or no note has been made by students on tuberculosis upon the healing of multiple miliary nodules within the spleen. The early stages of the development of the miliary tubercle is well known and has been much studied. These stages have been accurately followed through the proliferative reactions and the process of caseation. The growth of fibroblasts in the periphery of the advanced nodules has also been discussed, but few have reported observations upon the subsequent fate of the tubercle.

In our earliest observations upon the shot-like, mustard-seed nodules in the spleen we were unconvinced of their tuberculous nature. The fully headed nodule with its concentric layers of fibrous tissue and sharp demarcation from the surrounding spleen pulp, suggested a thrombotic origin of the fibrosis not unlike the formation of phleboliths in the pampiniform plexus of the testis. A further study, however, has given us an opportunity of seeing these nodules in the various stages of fibrosis. The lesions can be followed from the late caseous miliary tubercle with its surrounding fibroblasts to the definite encircling of the area with firm strands of connective tissue. Furthermore in some of the foci with advancing fibrosis evidence of the tuberculous process could be observed on the periphery in immediate contact with the sclerosing ring.

Autopsy No.	Sex.	Age.	Tuberculosis in organs.	Weight of spleen.	Fibrosis in spleen.	Nodules in spleen.	Previous history.
6	M.	42	Obsolete peribronchial glands and spleen	900	Fibrosis	One small calcareous	History of tuberculosis in family. Died of cirrhosis of liver.
16	M.	26	Obsolete spleen and liver	664	Adhesions	Numerous small hard and yellow nodules	No history of tuberculosis. Died of lobar pneumonia.
38	M.	42	Obsolete spleen.	95	Fibrosis.	Many small hard nodules, and one 0.75 cm.	No history of tuberculosis. Died of heart, kidney and arterial diseases.
40	M.	42	Obsolete peribronchial glands and spleen	260	None	Occasional small calcareous nodules	No history of tuberculosis. Died of pyemia.
51	M.	37	Obsolete tracheal glands, spleen and liver	240	Adhesions	Occasional small calcareous nodules and one in accessory spleen	History of tuberculosis not given. Died of chronic empyemia.
98	M.	61	Obsolete peribronchial, mesenteric glands, spleen and liver. Obsolescent lungs and peribronchial glands	165	Fibrosis	Several small hard yellow nodules	No history of tuberculosis. Died of pernicious anemia.
103	M.	64	Obsolete spleen	160	Fibrosis	One small hard yellow nodule	Died of heart, kidney and arterial diseases.
105	M.	63	Obsolete lung, peribronchial glands, spleen and liver	75	None	Many small hard nodules	No history of tuberculosis. Died of apoplexy (arteriosclerosis.
107	M.	23	Obsolete lung, peribronchial glands, spleen and liver	70	None	Several small hard nodules	Died after severe accident.
122	M.	53	Obsolete peribronchial glands and spleen	140	None	Two small hard nodules	No history of tuberculosis. Died of gonorrheal polyarthritis.
134	M.	43	Obsolete lungs, peribronchial glands & spleen. Obsolescent lungs & retroperitoneal glands	215	None	Many small calcified nodules	Pneumonia two years previously. Died of acute lobar pneumonia.
140	M.	42	Obsolete liver, spleen and mesenteric glands	350	None	Two small calcified nodules	Died of cancer of duodenum.
152	M.	36	Obsolescent lung; obsolete liver and spleen	750	Adhesions	Many hard calcareous nodules	Died following railroad accident.
169	M.	48	Caseous tuberculosis of lungs with cavitation. Obsolete spleen and liver	90	None	One hard shot-like nodule	Died of chronic pulmonary tuberculosis.
173	M.	69	Obsolete lungs, peribronchial glands, liver and spleen	95	None	Occasional small calcareous nodules	Died of fracture of skull.
180	M.	43	Obsolete spleen	150	Adhesions	Two small hard yellow nodules	No history of tuberculosis. Died of acute toxic jaundice.
201	M.	26	Obsolete spleen	?	Adhesions	Many small calcified nodules	Died of diphtheria.
223	M.	20	Obsolete liver and spleen	130	None	Many small seed-like bodies	Died of acute nephritis.
242	M.	21	Obsolete spleen	225	None	Two firm nodules with pin-point areas of necrotic tissue in center	No history of tuberculosis. Died of bronchiectasis and abscess of lung.
298	M.	49	Obsolete spleen	85	None	Single firm yellow nodule	No history of tuberculosis. Died of acute lobar pneumonia.
300	M.	28	Obsolete spleen	190	None	Single hard nodule with necrotic center	No history of tuberculosis. Died of acute lobar pneumonia.
308	F.	39	Obsolete peribronchial glands and spleen	195	None	Many small hard nodules.	No history of tuberculosis. Died of operative hematoma.
315	F.	70	Obsolete lung and spleen	75	Fibrosis	Some small shot-like nodules	History of chronic bronchitis. Died of bronchopneumonia.
333	F.	50	Obsolete spleen	140	Adhesions	Several small calcareous nodules	Died of acute lobar pneumonia.
349	M.	52	Obsolete spleen	200	Fibrosis	One small firm nodule	No history of tuberculosis. Died of syphilitic cirrhosis of liver.

Autopsy No.	Sex.	Age.	Tuberculosis in organs.	Weight of spleen.	Fibrosis in spleen.	Nodules in spleen	Previous history.
350	M.	30	Tuberculous bronchopneumonia. Obsolete and obsolescent peribronchial glands. Acute miliary lungs, spleen and liver. Obsolete spleen	390	None	Many small hard yellow nodules and many gray miliary tubercles	No previous history of tuberculosis. Died of acute miliary tuberculosis. Illness ten days simulating typhoid.
353	M.	25	Obsolete spleen	175	Adhesions	Many firm nodules with calcification	Died of Hodgkin's disease.
359	F.	18	Obsolete peribronchial glands spleen and lung. Obsolescent peribronchial glands	130	None	Several hard fibroid nodules size of mustard seeds	No history of tuberculosis. Died of acute gastro-enterocolitis.
360	F.	54	Obsolete peribronchial glands and spleen	115	None	One fibrosed nodule	No history of tuberculosis. Died of ebronic cholecystitis.
413	M.	36	Caseous tuberculosis of lung with cavitation. Obsolescent peribronchial glands and intestine. Obsolete liver and spleen	225	None	Several hard calcified nodules, the size of mustard seeds	Died of chronic tuberculosis and pyopneumothorax.
422	M.	28	Obsolescent peribronchial glands and lung. Obsolete lung and spleen	90	None	Several small hard nodules, size of mustard seeds	Died of acute lobar pneumonia.
478	F.	36	Obsolescent peribronchial glands Obsolete liver and spleen	195	Adhesions	Numerous round yellow white nodules	Died of rupture of uterus.
480	M.	35	Acute tuberculous peritonitis. Obsolescent peribronchial, retroperitoneal and omental glands, prostate and lung. Obsolete lung, spleen, liver and adrenal	?	None	Several hard round nodules	Died of tuberculous peritonitis.
516	M.	40	Obsolescent lung. Obsolete spleen and liver	250	None	Several small yellowish nodules	Died of acute lobar pneumonia.
522	M.	63	Obsolete peribronchial and mediastinal glands, and spleen. Acute miliary lung, kidney & spleen. Tuberculous ulcer of larynx	85	None	One small hard calcified nodule	Died of miliary tuberculosis.
534	M.	49	Obsolete spleen	125	None	Many fibrous and calcified nodules size of mustard seeds	Died of acute alcoholism and pneumonia.
541	F.	47	Caseous tuberculosis of lung with cavitation. Obsolete lung, peribronchial and mesenteric glands & spleen	125	None	A single firm white nodule	History of tuberculosis in family. Died of chronic tuberculosis.
567	M.	45	Obsolete spleen	360	None	Few small hard nodules	No history of tuberculosis. Died of appendicitis and peritonitis.
582	F.	42	Obsolescent peribronchial glands and adrenals. Obsolete peribronchial glands liver and spleen	?	None	Several small hard yellow nodules	Died of Addison's disease.
P-2898	F.	55	Obsolete spleen	175	Fibrosis	Several hard yellow nodules	History of cholelithiasis, jaundice, operation; death from hemorrhage.

To the naked eye the obsolete lesion is characteristic. The shot-like yellow nodules stand in strong contrast to the spleen pulp. The sharp demarcation without an infiltrating fibrosis differentiates the lesion from other sclerosing processes. However, it is impossible by the naked eye to state whether such discrete nodules are fully healed or are only in the obsolescent stage. We have found that nodules, hard and shotty, may still contain within them small remains of caseous material or even evidence on the outer border of a reaction suggesting a still active process. It is, of course, possible that the nodules with peripheral reaction have become the site of a new infection.

The material forming the basis of this report was obtained from 404 autopsies on individuals over ten years of age. In this series of autopsies particular attention was given to noting the presence of tuberculous foci in all parts of the body. Out of the entire series, tuberculosis was noted in 172 cases. The spleen was involved in a tuberculosis process in 69 cases. Of these there were 40 instances in which healed or almost completely healed tuberculous lesions, subsequently to be described, were found.

Of the 40 cases there were 31 males and 9 females. The average age was forty-two, the youngest being eighteen and the oldest seventy. In all but 12 cases old tuberculous lesions were found elsewhere, most frequently in the peribronchial lymph glands or in the lung. In the majority of instances the individual did not suffer from active tuberculosis and clinically no evidence of such infection was observed. Three patients, however, showed a persistent or chronic tuberculosis of the lungs; another died of tuberculous peritonitis, while 2 others died of an acute miliary tuberculosis. Other than these 6 cases the tuberculous lesion or lesions which were present elsewhere than the spleen were in the obsolete or obsolescent stage. In 28 cases an old tuberculous lesion outside of the spleen was found, and in the 6 cases suffering from active tuberculosis this antedated the recent dissemination. An interesting finding was the presence of healed miliary tubercles in the liver. Of these there were 15 cases, in 2 of which the liver and spleen were the only organs involved. These healed tubercles of the liver closely resembled those found in the spleen. They were small, round, and shot-like, without evidences of active tuberculosis in the organ.

Other than the characteristic tuberculous nodules in the spleen, this organ varied very much in its appearance. In weight it ranged from 76 to 900 grams. The average weight was 219 grams while there were twenty-four below 200 grams. As the finding of the old tuberculous lesions in the spleen was in the majority of cases only incident and as the individuals had died of various infections and accidents, the characters found within the spleen cannot entirely be referable to the old tuberculous lesions. It would appear from our

table that the presence of this tuberculous process has no marked influence upon the weight of the organ. The presence of fibrous adhesions about the spleen or of an increase of the fibrous tissue within the spleen, was noted in 15 cases. Such fibrosis or adhesions may have been associated with the acute stage of the tuberculous infection; however, all of these changes cannot be referred to the tuberculous process alone, as cirrhosis of the liver and chronic infections probably played a part in changing the structural character of this tissue. There were many instances in which no characteristic change was to be noted in the splenic structure other than the isolated fibrous nodules of old tuberculosis. In 2 cases the old and discrete tuberculous processes of the spleen were associated with more recent miliary tubercles in the active and progressive stages. This would indicate a second dissemination of tubercle bacilli reaching the spleen.

The miliary tubercle of the spleen in the healed or almost healed state differs quite markedly in its appearance from similar lesions in other organs save the liver. It appeared in the character of a small nodule of hard consistence and usually spherical. The type most commonly met with appeared like a small yellow concretion about the size, shape, and color of a mustard seed. Occasionally larger nodules were found, of somewhat irregular shape and measuring up to about 0.75 cm. in diameter. These nodules were irregularly scattered through the spleen substance, and their yellow color was in sharp contrast to the dark red pulp of the organ. They were found directly beneath the capsule or sprinkled through the parenchyma of the spleen. Their outer border was sharply demarcated from the spleen tissue, and they are quite easily removed from the surrounding structure. In their periphery there was no evidence of fibrosis extending into the surrounding parts. At times in shelling out the nodules the outer capsule was found to remain in the spleen tissue forming a small cup-like cavity. The discrete character of the nodules and the absence of change in their immediate vicinity was always striking.

The number of these nodules varied from a few to a large number. Occasionally small clusters were found, but in the majority of instances the discrete masses were irregularly scattered at some distance from each other. The macroscopic appearance of the tissues forming the nodules have been fairly uniform. They were hard and shot-like, and the outer coats consisted of concentric layers of fibrous tissue which could be removed in successive laminæ. The centers of the nodules were either hard and calcareous or fibrosed, some of them still showing soft necrotic material. The necrotic substance when present formed very small, almost pin-point areas in the immediate center. In a few instances a relationship between the nodules and the vascular channels was observed.

The finding of 12 cases in which tuberculous foci were alone

found in the spleen is remarkable. At first sight one would be tempted to suggest that the finding was dependent upon a careless search for otber lesions. In a number of cases, however, a distinct note was made at the time of autopsy that this was the only focus discovered. In these cases the splenic lesions differed in no way from those found in the remaining series.

There is one common characteristic possessed by all of the nodules which we have examined. This consists of the mature concentric layers of connective tissue which surround them and sharply demarcate the nodule from the spleen pulp. The spleen tissue immediately

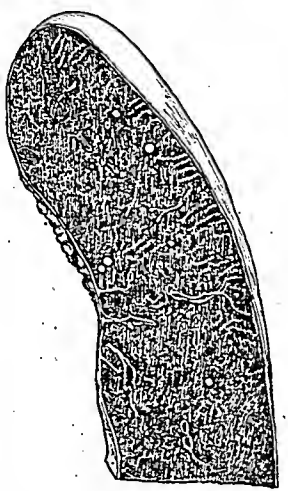

FIG. 1.—Spleen with obsolete miliary nodules of tuberculosis.

beyond the outer border of the nodule commonly showed no evidence of reaction, nor was its architecture changed. The fibrous tissue in the nodule did not send any trabeculæ into the surrounding tissue. This sharp line of demarcation in the absence of any response in the spleen pulp was quite remarkable. In some of the more recent lesions, those that had not advanced to complete healing showed more or less lymphocytic infiltration in the tissues immediately surrounding the nodules, and in 4 instances this was accompanied by the presence of small and recent tubercles in the progressive and active stages. In some cases it appeared that these

tubercles were associated with and dependent for their existence upon the main tubercles which had not reached the final stage of healing. In 2 instances recent tubercles were found in the spleen

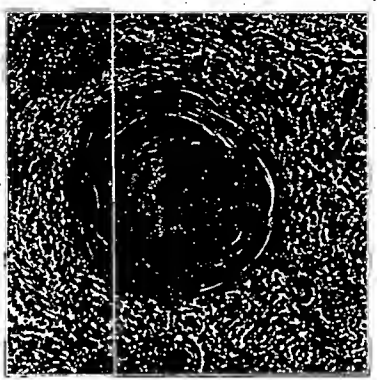

FIG. 2.—Fibrosed nodule with remnants of central necrosis.

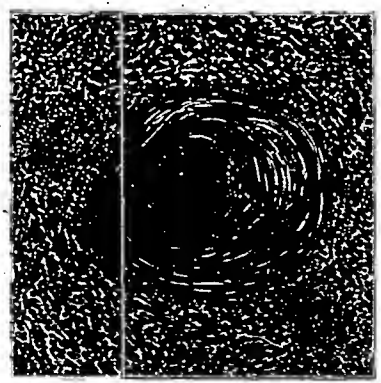

FIG. 3.—Fibrosed nodule with central calcification.

quite unassociated with the old nodules, but indicating a new hematogenous miliary distribution, as was indicated in the generalized miliary tuberculosis found elsewhere.

The size of the obsolete tuberculous lesions of the spleen indicated that during the active stage they consisted not of a single tubercle but of several closely approximated lesions. It is probable that, like the development of the ordinary miliary tubercle, the process began in a single tubercle, but with the development of necrosis and the multiplication of the tubercle bacilli a number of new tubercles were developed in the periphery. Thus numerous tubercles developed upon the circumference of the enlarging area until a size was attained which was readily distinguished by the naked eye.

The disposition of these old foci in the spleen was irregular and at times difficult to define. In some of them the remains of the central artery of the Malpighian body could still be seen within the fibrosed tubercle. These arteries were still patent and the fibrous tissue immediately bounding them was disposed in a direction concentric with the vessel. At other times it appeared as if the tubercle had developed within the pulp substance at a distance from the Malpighian body and unassociated with the trabeculæ of the spleen.

Although the nodules have, on naked-eye examination, a very similar appearance, and though they all have the common characteristic of being surrounded by a dense laminated connective tissue the central area may differ quite widely. In some the concentric layers of connective tissue continued throughout the nodule; others contained a small mass of granular necrotic material; the remains of former caseation in the center. The latter showed no evidence of an active process insofar as a tissue reaction was concerned. The necrotic material was firmly bounded by a wide border of dense connective tissue without evidence of lymphocytes, endothelial cells, or giant cells. A varying amount of calcification was also seen in these areas of necrosis. At times this consisted of a fine granular precipitate while in others a definite concretion formed a central nucleus.

The manner of laying down of the connective tissue is interesting. In the early development of the miliary tubercle in the spleen the proliferative response giving rise to the new cells of the tubercle leads to the crowding aside of the essential tissues of the area. The fine reticular stroma with its lymphocytes and endothelial cells is pushed outward, so that in the immediate periphery of the tubercle they appear to lie in a concentric fashion. At this early stage there is no increase in this reticular tissue. Soon, however, this neighboring stroma without actual proliferation increases the thickness of its strands by the accumulation of hyalin or collagen. It has thus been not uncommon to find a peripheral border of a heavy collagen containing connective tissue forming a lacework surrounding the tubercle, from which the lymphocytes gradually disappeared. When the lymphocytes accumulate it is usually to the outer side of this stroma. This connective-tissue boundary continues to exist with the increasing growth of the tubercle, but not until a reparative

process appears about the active foci does the original connective-tissue capsule increase to any definite degree. The laying down of new connective-tissue bands takes place on the inner side of this connective-tissue layer. Fibroblasts make their appearance in the small tubercles bounding the caseous center and gradually the characteristic architecture of the tubercle becomes disturbed until the giant cell lying within the jumble of fibroblasts and a few endothelial cells is all that remains of the active granuloma As the fibroblasts gradually lay down the permanent collagen fibers they are disposed in a concentric fashion. The disappearance of the fibroblast itself is rapid until nothing remains save the dense laminated collagen fibers. It was very apparent in these nodules that after the disappearance of the active process the new growth of connective tissue advanced but slowly. The caseous material in the center gave no evidence of tissue stimulation, and its absorption and removal was a slow procedure. Thus advancing fibrosis toward the center was a matter of time during which the central débris was being slowly removed.

Many sections of the fibroid masses, as well as of nodules with small caseous centers, were searched for tubercle bacilli but none were found. I would place no individual stress upon the negative finding obtained in material which had been stored in preservatives for more than a year, but as we have had similar results in dealing with tissues of more recent origin, I am inclined to view these structures as devoid of infection. At what stage in the healing process the microörganismas are destroyed cannot be stated, but it is probable that the event bears comparison with similar lesions in the lymph glands, as has been described by Warthin.

In 2 cases of recurrent infection of the spleen we have demonstrated tubercle bacilli in the progressive tissue lesions lying outside of the hard nodules, while no bacteria were found in the healed lesion. As we have previously stated these peripheral tubercles may have been a hematogenous reinfection of the spleen, or it may be that the bacteria had escaped from the primary miliary foci during the earlier stages of their development. In the latter case, if true, the infection remained latent over a considerable period, so that the difference in the tissue reaction between the primary and secondary lesion was very apparent.

Discussion. The evidence that we have here presented of healed or healing miliary tuberculosis of the spleen has an interest both from the clinical and pathological view-point.

In the majority of the cases the distribution of the tubercle bacillus to the spleen had taken place from small foci having no clinical significance. The findings indicate that the peribronchial glands were most frequently the areas from which microörganisms were disseminated by way of the blood stream. It is probable that, at the time of the bacillary distribution, several organs became

the point of localization, and we have evidence that in 15 cases the liver was simultaneously involved with the spleen. In the majority of instances, however, miliary lesions of contemporary infection were lacking elsewbere. It is obvious that scattered miliary lesions induced in many tissues escape our eye after the process of bealing is complete and when the local damage is of small extent. We cannot claim that in our series of autopsies all cases of healed miliary lesions of the spleen were observed, as isolated nodules may readily escape detection. It is, bowever, striking that as many as 40 cases should have come to our notice in a series of 404 autopsies on individuals over ten.

The absence of clinical data of any symptoms, wbereby the time of infection of the splenic tissues can be indicated, gives us no opportunity of determining the age and rapidity of the bealing process of localized miliary tuberculosis of the spleen. The early fibrosis developing about tuberculous areas after a period of six weeks or several months bas been well studied in man and animals. Sucb reactionary fibroses, bowever, are still in the proliferative stage when fibroblasts and young connective-tissue cells are laying down an outer wall about the area of necrosis. The majority of lesions in our cases, bowever, were much more advanced and were devoid of evidence of active proliferation except in the instances wbere more recent recurrent infection had localized in the vicinity of the old lesion. The concentric bands of connective tissue were in the mature state, and in some instances in a process of hyaline transformation. Months of time would bring little alteration in their structure. It is well seen that such encapsulation would permit only of slow organization of remnants of the caseous process. In some instances calcification of the central area supervened but in others a fine and granular necrotic material still remained. Whether any infection was still present in the central areas of necrosis could not be finally determined. We were unable to demonstrate tubercle bacilli in this material, but wbether latent infection was still available must remain unanswered until inoculation experiments are undertaken. As the material with which we were dealing had been preserved from autopsies performed at different times in the past five years, we were unable to carry out all of the studies necessary to clear up many of these points.

A point worthy of comment is that the presence of these old tuberculous foci had no marked effect upon the uninvolved portion of the spleen. In a number of cases adhesions were found; in a few others there was fibrosis. By no means, however, was the fibrosis marked and often when noted it was more relative than real. Furthermore, in some cases the fibrosis had a direct relation to an intercurrent disease process. Likewise there was no constant evidence of splenic enlargement resulting from the presence of old tuberculosis. It has been indicated that in the so-called primary

tuberculosis of the spleen one of the not unusual manifestations is the increase in weight and volume of the organ. The reported cases of primary tuberculosis of the spleen were observed in the acute or obsolescent stage. In these instances the focus of infection was of fair size, often occupying n considerable portion of the organ. Under these conditions the spleen showed definite enlargement. It is not uncommon that in acute miliary tuberculosis in which the spleen among other organs becomes the site of innumerable tubercles, its weight is materially increased. It may well be that during the acute process of infection of the cases reported in our series, the spleen was more or less enlarged. The condition, however, was transient leaving no characteristic organic change in its internal structure.

The distribution of the tuberculous infection was hematogenous. Whether the primary portal of entry was through the respiratory or alimentary system is immaterial. Undoubtedly, however, the infection primarily found localization in some other tissues where, after multiplication of the microörganisms and destructive changes in the involved structure, the bacteria found entrance into the blood stream. That no fatal outcome resulted at the time of this blood-stream dissemination indicated that relatively few bacteria were discharged from the initial focus. We have interesting evidence, therefore, that the quantity of infection of miliary tuberculosis varies greatly, and that the outcome of such distribution depends upon the relation between the amount of infection and the resistance of the tissues in which the bacteria locate. In these cases of old tuberculous foci in the spleen we have observed encapsulated nodules varying in number from one to very many.

A considerable interest has recently been taken in the role of the lymphocyte in tuberculosis. Bartel believed that he was able to demonstrate, by experiment, that a direct antagonism existed between lymphatic tissues and the tubercle bacillus. Primarily, it was found that a hyperplasia of the lymphoid structures along with an endothelial proliferation took place. These lymphatic tissues not only act as filters for the microörganism, but also offer a protective mechanism for the body. In many instances the infection of animal tissues by the tubercle bacillus is unassociated with structural change, even though the microörganisms are present in the tissues. Bartel has been able to demonstrate the tubercle bacillus within lymph glands in which no other change than hyperplasia had occurred. These bacteria he found were much reduced in virulence. Lewis and Margot found that there was a relation between the function of the spleen and the resistance of an animal to tuberculosis. Commonly after the inoculation with tubercle bacilli the spleen became enlarged. In mice it was found that splenectomy prolonged the life of the inoculated animals. No explanation could be offered for these apparently divergent results.

Ths importance of the spleen in counteracting infection, not only within its own tissue but also of a systemic kind, was shown in the experiments of Hektoen and of Simonds and Jones. These authors brought about partial destruction of the spleen by the application of the roentgen ray. After intense or prolonged exposure the animals developed a greater susceptibility for infection. This susceptibility appeared to be the result of a decrease in the lysins of the blood as well as a decided inhibition in the production and activity of the leukocytes. However, as the use of the roentgen-ray on small animals is not limited in its influence upon the spleen alone, it is possible that the change in the quantity of immune bodies is also dependent upon the effect of the rays upon the other hemopoietic organs. Somewhat more confusing results have been obtained by the use of benzol. This substance has a marked influence in depressing the production of leukocytes by the bone marrow, at the same time it was shown by White that prolonged treatment of rabbits by benzol led to the development of a much enlarged spleen. This occurred even when the leukocytes of the blood had been reduced more than one-half. Under these conditions of an enlarged spleen and diminished leukocytes the animal showed an increased susceptibility to the tubercle bacillus as compared to the untreated animals.

There appears, therefore, to be good evidence that the spleen has a definite relation to the development of immune bodies in various animals. This function is probably a limited one, and is similar to that possessed by other hemopoietic tissues. Whether the resistance of the spleen to infection differs greatly with the various microörganisms is not clear, but it would seem that, like other lymphatic tissues, its antagonism to the tubercle bacillus is quite marked.

Of the 40 cases of healed miliary tubercles of the spleen, 15 showed similar lesions in the liver. The liver nodules were identical with those in the spleen, being round and hard and of the size of mustard seeds. They were distributed irregularly through the liver substance, and usually were few in number. More frequently they were found in the peripbery of the lobule, in direct contact with the fibrous tissue of the portal systems. Their sharp demarcation from the surrounding liver tissue was as striking as in the spleen, and the absence of associated tissue change in other parts of the liver was constant. Whether the microörganisms located in the liver at the time of the general hematogenous distribution, or whether the liver infection was gained by the portal blood from the spleen cannot be stated. Both routes of infection are available, and a portal distribution during the active process in the spleen might readily occur.

In view of the high incidence of liver infection in all cases of tuberculosis, as is claimed by some, it is remarkable that healed miliary

nodules do not appear more frequently. If, as Ullom states, tuberculosis of the liver develops in from 70 to 100 per cent. of the cases, the mode of distribution must in large part be hematogenous, and Rolleston believed mainly by the portal vein. In our own observations we have failed to find tuberculosis of the liver as frequently as stated, though we have never undertaken a systematic search by the microscope. As is observed by all, the tuberculous lesions of the liver are most often of insignificant size and discovered only by microscopic search. The lesions which we have observed associated with the spleen nodules were all recognized by the naked eye at the autopsy table. Their character was so uniformly similar to those in the spleen as to suggest a synchronous deposition. Moreover, they would also indicate a tissue resistance to this infection equal to that of the spleen, suggesting a systemic as well as a local organic origin for the immunity. In no instance where healed miliary tubercles were found in the spleen had the liver infection progressed to conglomerate tubercles or cavitation. Even in those cases of pulmonary tuberculosis in which the tissue progressed to caseation and cavitation of the lungs the foci in the liver and spleen remained small and were well advanced in healing. These differences in the healing process of various tissues offer interesting studies in tissue immunity.

We find but little reference in the literature to the presence of healed miliary lesions in the spleen. Abbott in the *Catalogue of the McGill Medical Museum* mentions one specimen presented by Adami of the character as we have described. In an analysis of 1000 autopsies Adami and McCrae found evidence of healed tuberculosis in 151 cases and of these, healed lesions were present in the spleen twice while obsolescent lesions were seen four times. Winternitz has given a very full review of the work on tuberculosis of the spleen, in which he makes particular reference to the so-called primary tuberculosis, a condition quite different from that which we have under discussion. The lesions described by him usually refer to large caseous masses which have led to much enlargement of the spleen to be recognized clinically. A considerable number of these cases were treated surgically by splenectomy. Although the spleen is spoken of as the seat of acute or subacute miliary infection no reference is made to the healed lesion. The frequency of splenic involvement in tuberculosis is given by Reinhold, who found tuberculosis of the spleen in 67 per cent. out of 428 cases of tuberculosis in children, and in 19 per cent. out of 836 cases in adults. In our own series of 404 autopsies tuberculosis was present 172 times and the spleen was involved in 69 cases. In 40 of the latter healed miliary lesions were found in the spleen, 2 of them showing a reinfection with a fresh crop of tubercles. Sternberg in a discussion upon peculiar types of tuberculosis with characters of pseudoleukemia noted the tendency to fibrous encapsulation of tuberculous processes in the spleen. Colet and Gallavardin referred

to the finding of partly sclerosed nodules in the spleen of a man, aged sixty years. The liver in this case also had nodules which were still caseous. The report on focal tuberculosis of the spleen by Fischer deals with subacute lesions in which caseation occupies the center of the nodule while the peripbery is made up of proliferating epithelioid and giant cells. None of the lesions observed by him bad reacbed the obsolete stage. Brohl excised the spleen of a patient aged forty-eigbt years, and found six small yellow concretions which contained calcium carbonate and phosphate, and which he believed had their origin in phleboliths.

More comparable to the described lesions of the spleen are those reported by Warthin occurring in the mesenteric glands. Warthin claimed to find evidence of healed tuberculosis in the mesenteric glands with great frequency. The tissue changes consisted in part of hyaline deposits as well as small fibrosed nodules with central débris and a peripberal laminated structure. The latter lesions appeared very similar to those which we have observed in the spleen. On no occasion, bowever, have we found the centers to consist of a hyaline substanec. The hyaline transformation of the neigbboring stroma was frequently observed in the spleen in the presence of tuberculous foci. Warthin found similar hyaline and sclerosed masses in the bronchial glands of adults.

A word must be said about the 12 cases of healed miliary tuberculosis of the spleen in which no other focus was found in the body. As we have previously indicated, search was made at the time of autopsy for other tuberculous manifestations, and none were found. We cannot but doubt that some unrecognized focus bad existed near the point of entrance of the infection, but that recognizable tissue change was no longer evident. The splenic infection had undoubtedly developed through blood infection in which other organs had also received localized foci. It would appear tbat the tuberculous process had been dealt with unequally in tbe various tissues, all save the spleen clearing themselves of the invading organism before permanent damage was done. In the spleen, temporary tissue destruction was brought about with subsequent complete healing. In these cases it would appear that the resistance of the spleen to tuberculous involvement was not so great as in öther tissues. These findings would indicate that a tuberculous bacteriemia may occur in the absence of an advanced localized focus of infection and that a miliary distribution may be overcome by the individual tissue resistance.

CONCLUSIONS. In a series of 404 autopsies, tuberculosis was met with in 172 cases. The spleen was involved 69 times, and in 40 of these miliary lesions were completely or almost completely healed by fibrosis.

The average age was forty-two years and the youngest was eigbteen years. Six of the cases showed a persistent tuberculosis in other organs. In 15 cases the liver also contained bealed miliary tubercles.

In none of the cases had there been recognizable clinical manifestations of splenic involvement. The spleen was not enlarged. In 12 cases with healed miliary tubercles of the spleen no other tuberculous process was found.

The splenic infection was a hematogenous one arising most commonly from antecedent foci in the lungs or peribronchial glands. Those cases in which no primary tuberculous focus was found probably had a similar mode of origin in which, however, the initial focus was of minor extent unrecognizable at the time of autopsy. We would point out that the fibroses which are observed in anthracotic peribronchial glands are difficult of analysis as indicating a preceding infectious origin of the fibrosis.

The healed splenic tubercles are recognized only by careful search and complete gross sectioning of the tissues of the organ. The presence of the healed miliary tubercles of the spleen indicates the frequency of a tuberculous bacteriemia from which the tissues may entirely recover. The different organs demonstrate a variable resistance to the tuberculous infection. Reinfection may take place in the spleen.

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THE ASSOCIATION OF GASTRIC SYMPTOMS IN NEPHRITIS WITH RETENTION OF NITROGENOUS WASTE PRODUCTS IN THE BLOOD.[1]

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Since the time of Richard Bright it has been recognized that renal disorders are accompanied by digestive disturbances. The

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